

# (12) United States Patent

Devane et al.

#### US 6,228,398 B1 (10) Patent No.:

(45) Date of Patent: May 8, 2001

## MULTIPARTICULATE MODIFIED RELEASE **COMPOSITION**

Inventors: John G. Devane; Paul Stark; Niall M. M. Fanning, all of Athlone (IE)

Assignee: Elan Corporation, PLC, Dublin (IE)

Subject to any disclaimer, the term of this Notice:

patent is extended or adjusted under 35

U.S.C. 154(b) by 0 days.

Appl. No.: 09/566,636

(22)Filed: May 8, 2000

### Related U.S. Application Data

- Continuation of application No. PCT/US99/25632, filed on (63)
- Provisional application No. 60/106,726, filed on Nov. 2,
- (51)
- **U.S. Cl.** ...... **424/484**; 424/464; 424/465; 424/468; 424/469; 424/456; 424/451; 424/472
- (58)424/462, 472, 464, 468, 484, 465, 469,

#### (56)References Cited

#### U.S. PATENT DOCUMENTS

4,728,512		3/1988	Mehta et al	424/458
4,794,001		12/1988	Mehta et al	424/458
4,888,178		12/1989	Rotini et al	424/468
4,904,476		2/1990	Mehta et al	424/456
5,158,177		10/1992	Abramowitz et al	424/458
5,445,829	*	8/1995	Paradissis et al	424/480
5,639,476	*	6/1997	Oshlack et al	
5,726,316	*	3/1998	Crooks et al	

#### 5,837,284 11/1998 Mehta et al. ...... 424/459

# FOREIGN PATENT DOCUMENTS

0 274 734 A1 7/1988 (EP). 0 274 734 7/1988 (EP). WO9703672 2/1997 (WO). WO98/14168 4/1998 (WO).

#### OTHER PUBLICATIONS

Shah, et al., J. Cont. Rel. (1989) 9:169-175. Giumchedi, et al., Int. J. Pharm (1991) 77:177-181. Conte, et al. Drug. Del. Ind. Pharm. (1989) 15:2583-2596.

\* cited by examiner

Primary Examiner—Thurman K. Page Assistant Examiner—Rachel Bennett (74) Attorney, Agent, or Firm—Kilpatrick Stockton LLP

#### **ABSTRACT** (57)

The invention relates to a multiparticulate modified release composition that in operation delivers an active ingredient in a pulsed or bimodal manner. The multiparticulate modified release composition comprises an immediate release component and a modified release component; the immediate release component comprising a first population of active ingredient containing particles and the modified release component compnsimg a second population of active ingredient containing particles coated with a controlled release coating; wherein the combination of the immediate release and modified release components in operation deliver the active ingredient in a pulsed or a bimodal manner. The invention also relates to a solid oral dosage form containing such a multiparticulate modified release composition. The plasma profile achieved by the multiparticulate modified release composition is advantageous in reducing patient tolerance to the active ingredient and in increasing patient compliance by reducing dosage frequency.

# 37 Claims, 1 Drawing Sheet

